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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/874,166	06/04/2001	William Thomas Melvin	12489-003002/UMMC Ref: UM	8129

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EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 10/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/874,166	MELVIN ET AL.	
	Examiner	Art Unit	
	Jon Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 May 2005 and 04 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-35 and 41-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-35 and 41-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/043,814.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection (8/4/2005). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/31/2005 has been entered.

Claims 27-35 and 41-44 are currently pending in the application and are addressed herein.

Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c). Specifically, the post office address of Michael Danny Burke has been altered, however, no the alterations have not been dated or initialed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 27-35 and 41-44 are rejected under 35 U.S.C. 112, first paragraph as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988).

Wands states on page 1404,
"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

It is noted that claim 27 is drawn to a method for activating T cells in a subject by administering to the subject an amount of a cytochrome P450 CYP1B1 sequence effective to activate T cells that recognize a CYP1B1 epitope. As indicated in the response filed 9/13/04 (see p. 4), "to require that a CYP1B1 sequence (such as a CYP1B1 amino acid sequence or nucleic acid sequence) be administered to the subject..." (Emphasis added). Therefore it is clear that the claim encompasses administering a nucleic acid sequence or an amino acid sequence to the subject.

It is noted that the claims encompass activating T cells in a subject that has cancer (claims 31, 32) wherein the method results in a cell-mediated or humoral immune response against the cancer (claim 33). Since claim 27 is the independent claim it must, by definition, encompass all limitations set forth in the dependent claims. Therefore, claim 27 (as well as all claims dependent on claim 27--i.e., all pending claims) must encompass a method of activating a cell-mediated or humoral immune response against a cancer in a subject. Therefore, all pending claims encompass treating cancer by administering a tumor antigen sequence (either nucleic acid sequence or protein sequence) to a subject having cancer. The claims are not enabled for the reasons set forth in previous Office Actions, which are reiterated below.

The nature of the invention

The claims are drawn to a method of activating T cells in a subject by administering a cytochrome P450 CYP1B1 sequence to the subject in an amount effective to activate T cells that recognize a CYP1B1 epitope, and includes stimulating an immune response against cancer cells. Therefore, the claims encompass cancer immunotherapy (e.g., treating cancer by administering a tumor antigen sequence), also known as cancer vaccination.

The breadth of the claims

The claims are very broad. The broadest claims encompass stimulating T cells in a subject by administering a cytochrome P450 CYP1B1 sequence to the subject in an amount effective to activate T cells that recognize a CYP1B1 epitope. The claims also explicitly encompass administering any CYP1B1 sequence (such as SEQ ID NOS 1 or 2) that activates said human T cells.

The unpredictability of the art and the state of the prior art

The state of the art, including the post-filing art indicates that cancer immunotherapy and gene therapy (which is encompassed by the claims because the claims encompass administering a CYP1B1 nucleic acid sequence) are not methods that can be predictably performed.

For instance, with respect to administering a nucleic acid to a subject (e.g., gene therapy) the relevant art recognizes a number caveats and obstacles that must be overcome before the method can be predictably performed without an undue amount of additional experimentation.

At the time of filing, the relevant art considered gene therapy as a whole to be unpredictable as modes of delivery that would provide efficient expression of genes encoding the therapeutic polypeptide (in this case the immunostimulatory amino acid sequence) sufficient to result in the desired effect, in this case activating T cells. Currently, the state of the art of gene therapy is still in its infancy as the art is plagued by unpredictability. For instance, Crystal (Science, 1995; 270:404-409) teaches, "All of the human gene transfer studies have been plagued by inconsistent results, the basis of which are unclear", and sites specific examples including inconsistent results, the inconsistency of results in animal models and humans, vector production problems, and vector efficiency (see page 409, columns 1-2). Specifically, regarding the ideal gene therapy vector, Crystal teaches, "The vector should be specific for its target, not recognized by the immune system, stable and easy to reproduce... Finally it would express the gene (or genes) it requires for as long as long as required in an appropriately regulated fashion." (See p. 409, second column).

Verma et al. (Nature, 1997; Vol. 389) teaches, "there is still no single outcome that we can point to as a success story" (see pg. 239, col. 1; Gene Therapy Promises, Problems and Prospects). More recently, Walther and Stein (2000) reaffirms the obstacles to successful gene

therapy by stating, "The hurdles to overcome in efficient gene therapy are successful gene transfer of the therapeutic genes, appropriate expression levels associated with sufficient duration of gene expression, and the specificity of gene transfer to achieve therapeutic effects in the patient." (See p. 267, under "Discussion"). Walther and Stein also indicate, "The majority of clinical trials using viral vectors for gene therapy in humans still lack a significant clinical success, defining the still existing barriers to achieving clinical benefits with gene therapy" (See pg.267, Discussion section).

To overcome the teachings in the art (with respect to administering a CYP1B1 nucleic acid sequence), the specification would need to supply direct, correlative guidance on how to administer the CYP1B1 nucleic acid to a subject in such a way that the nucleic acid is delivered to an appropriate cell such that the nucleic acid expresses the CYP1B1 amino acid sequence in the cell, that the amino acid sequence is properly expressed (e.g., at an appropriate level for an appropriate duration of time and secreted from the cell in an effective amount) such that administration of the sequence effectively activated T cells in the subject such that method resulted in an effective immune response against a cancer in the subject.

With respect to cancer immunotherapy, the relevant art recognizes a number caveats and obstacles that must be overcome before cancer immunotherapy methods can be can be predictably performed without an undue amount of additional experimentation.

For instance, Bodey et al. (2000; previously cited) teaches: "The cancer vaccine approach to therapy is based on the notion that the immune system could possibly mount a rejection strength response against the neoplastically transformed cell conglomerate. However, due to the

low immunogenicity of tumor associated antigens, down regulation of MHC molecules, the lack of adequate co-stimulatory molecule expression, secretion of immune inhibitory cytokines, etc., such expectation are rarely fulfilled...faulty antigen presentation which could result in tolerance induction to the antigens contained within the vaccine, and subsequent rapid tumor progression." (Page 2665, column one).

Additionally, Gouttefangeas et al. (2000; previously cited) teaches,

> "As most cancer patients obviously do not mount efficient T cell responses against their tumors, the task is clear: immunotherapies must induce cancer-destroying T cells in patients. Although this goal appears straight forward, effective immunotherapy has remained elusive because of three major problems: first, for many tumors, no or not enough suitable antigens are known; second, no consensus exists for the best antigen formulation or the route of immunization; and third, tumors under immune attack tend to be selected for antigen loss variants." (See p. 491, first column).

Thus, Gouttefangeas indicates that patients that have tumors which express the tumor antigen do not mount an efficient immune response to these tumors. Therefore, administering a tumor antigen to a patient comprising a tumor that expresses the antigen may not be sufficient to activate an immune response to the human tumor antigen. Furthermore, Gouttefangeas indicates that a single tumor antigen may not be sufficient to activate an effective immune response to the tumor. It is noted that the instant specification has only described epitopes of a single tumor antigen, human CYP1B1. Finally, Gouttefangeas teaches that using immunotherapy for cancer treatment is unpredictable because the treatment can select for tumor cells that do not express the tumor antigen, thus rendering the treatment ineffective in tumors that comprise cancer cells that do not express the antigen.

Furthermore, Radoja et al. (Mol Med 2000; previously cited) teaches that cancer-induced defective cytotoxic T lymphocyte is probably another mechanism how tumor antigen escape immune surveillance. Specifically, Radoja teaches,

> "THE NOTION THAT A DEFICIT IN IMMUNE CELL FUNCTIONS PERMITS TUMOR GROWTH HAS RECEIVED EXPERIMENTAL SUPPORT WITH THE DISCOVERY OF SEVERAL DIFFERENT BIOCHEMICAL DEFECTS IN T LYMPHOCYTES THAT INFILTRATE CANCERS" (abstract). "ACCUMULATION OF CIRCULATING ANTITUMOR IMMUNOGLOBULIN G IN CANCER PATIENTS SHOW THAT THE PRIMING PHASE OF ANTITUMOR IMMUNE RESPONSE IS FUNCTIONAL DURING THE RELATIVELY SLOW PROCESS OF NASCENT TUMOR GROWTH...IN BOTH HUMAN CANCER PATIENTS AND RODENTS BEARING TUMORS OF DIFFERENT HISTOLOGIC ORIGIN, SYSTEMIC IMMUNITY IS NOT PROFOUNDLY SUPPRESSED..." "HOWEVER, INHIBITION OF A SPECIFIC ANTITUMOR IMMUNE RESPONSE HAS BEEN OBSERVED FREQUENTLY. A VARIETY OF MECHANISM HAVE BEEN PROPOSED TO ACCOUNT FOR DEFECTIVE ANTITUMOR IMMUNE RESPONSE, INCLUDING: SECRETION OF SUPPRESSIVE FACTORS IN THE TUMOR MICROENVIRONMENT, THE LACK OF EXPRESSION OF COSTIMULATORY SIGNALS ON TUMOR CELLS, INDUCTION OF REGULATORY T CELLS HAVING A SUPPRESSIVE PHENOTYPE, LOSS OF ANTIGEN PRESENTATION FUNCTION IN THE TUMOR, LOSS OF EXPRESSION OF HLA CLASS I ANTIGEN PRESENTING MOLECULES IN TUMORS, TUMOR-INDUCED T-CELL SIGNALING DEFECTS, LOSS OF TUMOR ANTIGEN EXPRESSION, IMMUNOLOGICAL IGNORANCE AND, SINCE MANY TUMOR ANTIGENS ARE EITHER UNMODIFIED SELF OR EPITOPES CLOSELY RELATED TO SELF, THE REDUCTION OF THE REPERTOIRE OF POTENTIAL HIGH AFFINITY ANTITUMOR T-CELL CLONES DURING T-CELL MATURATION IN THE THYMUS" (Introduction).

Thus, it is evident that the skilled artisan, while acknowledging the significant potential of immunotherapy for cancer, still recognizes that such therapy is neither routine nor wholly accepted. Furthermore, significant development and further guidance is necessary for its practice. Therefore, it is incumbent upon applicants to provide sufficient and enabling teachings within the specification for the instant methods.

In order to enable the instant claims in light of the state of the relevant art, the applicant must provide guidance/working examples to demonstrate that the CYP1B1 epitopes are highly

immunogenic and could provoke a useful immune response without the problems in the cited references or must provide ways to overcome the cited difficulties.

Working Examples and Guidance in the Specification

The specification does not have any working examples that indicate that a CYP1B1 sequence (including a CYP1B1 nucleic acid sequence and a CYP1B1 amino acid sequence comprising SEQ ID NO:1 or SEQ ID NO:2) can be used to: (1) activate T cells in a subject; and/or, (2) stimulate an immune response against a cancer in a subject. The only examples provided indicate that the human CYP1B1 epitopes disclosed (specifically, the amino acid sequences consisting of SEQ ID NO:1 and SEQ ID NO: 2) can be used to raise antibodies against the epitopes in mice. As indicated above activating T cells in a subject and stimulating an immune response against a cancer using a tumor antigen epitope is not a matter of routine experimentation.

Quantity of Experimentation

Considering the breadth of the claims, and the unpredictability of gene therapy and cancer immunotherapy recognized in the art, additional experimentation is required in order for one of skill in the art to be able to practice the claimed invention. Considering the lack of working examples or guidance in the specification and also considering the teachings of the relevant art that the required experimentation is not routine, the amount of additional experimentation required is deemed to be undue.

Level of the skill in the art

The level of the skill in the art is deemed to be high.

Conclusion

Considering the high degree of unpredictability of gene therapy and cancer immunotherapy recognized in the art, the breadth of the claims, the lack of working examples and guidance in the specification, and the high degree of skill required, it is concluded that the amount of experimentation required to perform the broadly claimed invention is undue.

Response to Arguments

Applicant's arguments filed 5/31/2005 have been fully considered but they are not persuasive.

Applicants submit that the Examiner noted that a showing that the administration of CYPIBI sequences to a subject (as indicated in the claims) could activate T cells and stimulate an immune response against cancer cells would overcome this rejection. Applicants contend that independent claim 27 is directed to a method for activating T cells in a subject by administering to the subject an amount of a cytochrome P450 CYP1B1 sequence effective to activate T cells that recognize a CYP1B1 epitope. Applicants contend that the working examples contained in the application as filed show that CYP1B1 is expressed in a wide range of tumors but not in the normal tissues that were tested. Applicants submit that as a result of this marked preferential expression of CYP1B1 in tumors, the specification teaches that CYP1B1 sequences can be used to immunize a subject, thereby resulting in activated T cells that recognize a CYP1B1 epitope and mediate an immune response against a CYPlBl-expressing tumor. Applicants assert that because of their experimental findings clearly showing that CYP1B1 is expressed in many types of cancers, but not expressed in those normal tissues studied, the person of ordinary skill in the art at the time of filing of the present application would have reasonably expected that CYP1B1

sequences could be used to generate an immune response against CYPlBl-expressing tumor cells. As confirmation that, as taught in the specification, CYP1B1 sequences can be used to generate an immune response against CYP1B1-expressing tumor cells, an article by Gribben et al. entitled "Unexpected Association Between Induction of Immunity to the Universal Tumor Antigen CYP1B1 (ZYC300) and Response to Next Therapy" ("Gribben") is enclosed with the present response. Applicants submit the Gribben confirms that (as detailed in the specification) CYP1B1 sequences can be used effectively as therapeutic compositions to stimulate an anti-CYP1B1 immune response and provide a clinical benefit to cancer patients.

In response, it is respectfully pointed out that in order for a claimed invention to be fully enabled, it must be enabled at the time of filing (see MPEP § 2164.05(a) "Specification Must Be Enabling as of the Filing Date"). It is noted that MPEP § 2164.05(a) specifically indicates:

> "Whether the specification would have been enabling as of the filing date involves consideration of the nature of the invention, the state of the prior art, and the level of skill in the art... The state of the art for a given technology is not static in time. It is entirely possible that a disclosure filed on January 2, 1990, would not have been enabled. However, if the same disclosure had been filed on January 2, 1996, it might have enabled the claims. **Therefore, the state of the prior art must be evaluated for each application based on its filing date**... The state of the art existing at the filing date of the application is used to determine whether a particular disclosure is enabling as of the filing date. Chiron Corp. v. Genentech Inc., 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1325-26 (Fed. Cir. 2004) ("a patent document cannot enable technology that arises after the date of application"). Publications dated after the filing date providing information publicly first disclosed after the filing date generally cannot be used to show what was known at the time of filing. In re Gunn, 537 F.2d 1123, 1128, 190 USPQ 402,405-06 (CCPA 1976); In re Budnick, 537 F.2d 535, 538, 190 USPQ 422, 424 (CCPA 1976)... While **a later dated publication cannot supplement an insufficient disclosure in a prior dated application to make it enabling**, applicant can offer the testimony of an expert based on the publication as evidence of the level of skill in the art at the time the application was filed. Gould v. Quigg, 822 F.2d 1074, 1077, 3 USPQ2d 1302, 1304 (Fed. Cir. 1987)." (Emphasis Added).

In the instant case, the specification does not provide an enabling disclosure for the claimed invention at the time of filing. It is acknowledged that the Examiner indicated in the Office Action mailed 11/30/2004, that a showing that the administration of CYP1B1 sequences to a subject (as indicated in the claims) could activate T cells and stimulate an immune response against cancer cells would overcome this rejection. However, in order to be perfectly clear, a showing that the administration of CYP1B1 sequences to a subject (as indicated in the claims) could activate T cells and stimulate an immune response against cancer cells based on the teaching of the specification and only requiring the knowledge of the art at the time of filing would overcome this rejection.

Since the specification must be enabling at the time of filing, any evidence presented to show that the specification is enabling for the claimed method should not rely on critical features that are not disclosed in the specification and which were not taught in the prior art. In the instant case, Applicants submit that the post filing art reference referred to as "Gribben" confirms that as detailed in the specification, CYP1B1 sequences can be used effectively as therapeutic compositions to stimulate an anti-CYP1B1 immune response and provide a clinical benefit to cancer patients. However, Gribben relies on critical features which were not disclosed in the instant specification and which were not taught in the prior art. Specifically, Gribben teaches that a plasmid which encodes an inactivated CYP1B1 DNA formulated within biodegradable poly-DL-lactide-coglycolide microparticles was administered to the subjects. The instant specification and prior art do not teach the inactivated CYP1B1 DNA or the biodegradable poly-DL-lactide-coglycolide microparticles used in the experiments performed by Gribben.

Furthermore, it is noted that Gribben teaches:

> "As a targeted therapy, cancer vaccines should not only kill cancer cells with limited toxicity but also generate ongoing antitumor responses secondary to development of immunologic memory and eradicate residual tumor. Because tumor antigens are largely autoantigens, the most significant obstacle is the requirement to overcome immune tolerance and emergence of antigen-negative tumor variants might further limit utility. In addition despite demonstration of development of immunologic responses, the clinical responses to vaccination trials have often been disappointing. Potential reasons for this include suppressive mechanisms within the tumor-bearing patient so that within the tumor microenvironment both soluble and cell-based immunosuppressive mechanisms seem to dampen or prevent the function of antitumor effector cells. **Strategies to overcome these obstacles are necessary before cancer vaccines become a clinical reality**." (Emphasis added, see page 1, first paragraph).

As such, Gribben teaches that even today (i.e., well after the filing date of the instant application), the state of the art with respect to cancer vaccines/cancer immunotherapy is unpredictable and additional experimentation is necessary. Therefore, Gribben affirms that the mere identification of a tumor antigen is insufficient to establish that the tumor antigen could be predictably used to activate T-cells and stimulate a therapeutic anti-cancer immune response in a subject without performing additional experimentation. It is noted that the instant specification merely identifies CYP1B1 as a tumor specific antigen and does not provide the guidance or working examples which are required to overcome the problems recognized in the cancer vaccine/immunotherapy art.

Furthermore, Gribben does NOT teach that CYP1B1 sequences can be predictably used to induce anti-CYP1B1 immunity. In fact, Gribben teaches that the CYP1B1 sequences were administered to 18 patients and 6 of these patients developed "immunity" to CYP1B1 (e.g., see abstract). Therefore, 12 of the 18 patients did not develop immunity. Furthermore 5 of the 6 patients which developed "immunity" required further salvage treatment for progressive metastatic disease (e.g., see abstract). Gribben teaches that it is not clear why 12 of the patients

did not develop immunity and why additional salvage treatment was required in 5 of the 6 patient which developed CYP1B1 immunity (e.g., see pages 5-7). Furthermore, Gribben teaches,

> "Whether the mechanism of response is immunologically mediated or whether the generation of anti-CYP1B1 immunity has biologically altered tumor cell resistance or the microenvironment, we believe that these results are of considerable interest and should be verified and further explored. We, therefore, present these data as a hypothesis to be addressed in ongoing and future tumor vaccine studies. Such studies should determine not only which patients develop immunity but also whether patients who develop immunity can be given additional therapy, including conventional antitumor drugs or agents that either enhance immunity or reverse immune suppression to induce clinically beneficial responses." (See page 7, second column)

Therefore, even in light of the teaching of Gribben, the use of CYB1B1 sequences to stimulate an effective T-cell response against cancer cells is, at best, unpredictable and further experimentation is required.

As such, the teaching of Gribben does not indicate that the instant specification provides a sufficient disclosure to enable the claimed method. Therefore, applicants' arguments are not persuasive and the rejection is maintained.

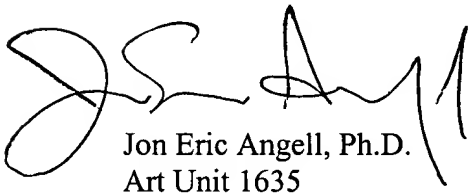
Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Mon-Fri, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Jon Eric Angell, Ph.D.
Art Unit 1635